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PASSWORD:
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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	MAR 31	IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats
NEWS 3	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
NEWS 4	MAR 31	CA/CAplus and CASREACT patent number format for U.S. applications updated
NEWS 5	MAR 31	LPCI now available as a replacement to LDPCI
NEWS 6	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 7	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS 8	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS 9	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS 10	APR 28	IMSRESEARCH reloaded with enhancements
NEWS 11	MAY 30	INPAFAMDB now available on STN for patent family searching
NEWS 12	MAY 30	DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option
NEWS 13	JUN 06	EPFULL enhanced with 260,000 English abstracts
NEWS 14	JUN 06	KOREAPAT updated with 41,000 documents
NEWS 15	JUN 13	USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications
NEWS 16	JUN 19	CAS REGISTRY includes selected substances from web-based collections
NEWS 17	JUN 25	CA/CAplus and USPAT databases updated with IPC reclassification data
NEWS 18	JUN 30	AEROSPACE enhanced with more than 1 million U.S. patent records
NEWS 19	JUN 30	EMBASE, EMBAL, and LEMBASE updated with additional options to display authors and affiliated organizations
NEWS 20	JUN 30	STN on the Web enhanced with new STN AnaVist Assistant and BLAST plug-in
NEWS 21	JUN 30	STN AnaVist enhanced with database content from EPFULL
NEWS 22	JUL 28	CA/CAplus patent coverage enhanced
NEWS 23	JUL 28	EPFULL enhanced with additional legal status information from the epoline Register
NEWS 24	JUL 28	IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
NEWS 25	JUL 28	STN Viewer performance improved
NEWS 26	AUG 01	INPADOCDB and INPAFAMDB coverage enhanced

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

NEWS HOURS STN Operating Hours Plus Help Desk Availability

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FILE 'HOME' ENTERED AT 08:05:01 ON 01 AUG 2008

=> FILE CAPLUS MEDLINE
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'CAPLUS' ENTERED AT 08:05:38 ON 01 AUG 2008
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FILE 'MEDLINE' ENTERED AT 08:05:38 ON 01 AUG 2008

=> ERUNGE HANS-JOACHIM/IN
ERUNGE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> E RUNGE HANS-JOACHIM/IN
'IN' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'MEDLINE'
E1            2     RUNGE HANS JUERGEN/IN
E2            1     RUNGE HANS JURGEN/IN
E3            0 --> RUNGE HANS-JOACHIM/IN
E4            1     RUNGE HARRY V/IN
E5           10     RUNGE HARTMUT/IN
E6            1     RUNGE HARTMUT DIPL ING/IN
E7            1     RUNGE HARTMUT DIPL PHYS DR RER/IN
E8            3     RUNGE HEIKO/IN
E9           26     RUNGE HENRICO/IN
E10           1     RUNGE HORST/IN
E11           1     RUNGE JAN MICHAEL/IN
E12           1     RUNGE JEAN R/IN
The indicated field code is not available for EXPAND in this
file.  To see a list of valid EXPAND field codes, enter HELP
SFIELDS at an arrow prompt (=>).

=> E RUNGE HANS/IN
'IN' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'MEDLINE'
E1            2     RUNGE GISELA/IN
E2            2     RUNGE H/IN
E3            0 --> RUNGE HANS/IN
E4            2     RUNGE HANS FRIEDRICH/IN
E5           22     RUNGE HANS JOACHIM/IN
E6            2     RUNGE HANS JUERGEN/IN
E7            1     RUNGE HANS JURGEN/IN
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E8            1     RUNGE HARRY V/IN
E9           10     RUNGE HARTMUT/IN
E10           1     RUNGE HARTMUT DIPL ING/IN
E11           1     RUNGE HARTMUT DIPL PHYS DR RER/IN
E12           3     RUNGE HEIKO/IN
The indicated field code is not available for EXPAND in this
file.  To see a list of valid EXPAND field codes, enter HELP
SFIELDS at an arrow prompt (=>).

=> S E5
'IN' IS NOT A VALID FIELD CODE
L1           22 "RUNGE HANS JOACHIM"/IN

=> E LEMBCKE ADALBERT/IN
'IN' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'MEDLINE'
E1            1     LEMBARIK FARID SALEM/IN
E2            1     LEMBAS JACEK/IN
E3            1 --> LEMBCKE ADALBERT/IN
E4            1     LEMBCKE ANDREAS/IN
E5            1     LEMBCKE EBERHARD/IN
E6            1     LEMBCKE GUENTER/IN
E7            2     LEMBCKE JEFFREY/IN
E8            3     LEMBCKE JEFFREY JOHN/IN
E9            7     LEMBCKE RALF/IN
E10           4     LEMBCKE RICHARD E/IN
E11           4     LEMBCKE ROBERT M/IN
E12           1     LEMBECK BERNHARD KARL PETER/IN
The indicated field code is not available for EXPAND in this
file.  To see a list of valid EXPAND field codes, enter HELP
SFIELDS at an arrow prompt (=>).

=> S E3
'IN' IS NOT A VALID FIELD CODE
L2            1 "LEMBCKE ADALBERT"/IN

=> S L1 OR L2
L3           22 L1 OR L2

=> S FLUTAMIDE OR EULEXIN OR FLUTAMIN
L4         4689 FLUTAMIDE OR EULEXIN OR FLUTAMIN

=> S MILL OR MILLING OR UNMILLED OR MILLED
L5       177751 MILL OR MILLING OR UNMILLED OR MILLED

=> S L4 AND L5
L6            5 L4 AND L5

=> D L6 1-5 IBIB ABS HITSRT
'HITSRT' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
CLASS ------- IPC, NCL, ECLA, FTERM
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
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FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
              SCAN must be entered on the same line as the DISPLAY,
              e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, CLASS

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
              containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
              its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
              its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

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an arrow prompt (=>).  Examples of formats include: TI; TI,AU; BIB,ST;
TI,IND; TI,SO.  You may specify the format fields in any order and the
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FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC
to view a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):IBIB ABS

L6   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2005:1042029  CAPLUS
DOCUMENT NUMBER:          143:312056
TITLE:                    Pharmaceutical formulation containing unmilled
                          flutamide
INVENTOR(S):              Runge, Hans-Joachim; Lembcke, Adalbert
PATENT ASSIGNEE(S):       Hexal A.-G., Germany
SOURCE:                   PCT Int. Appl., 32 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
```

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005089711	A2	20050929	WO 2005-EP2884	20050317
WO 2005089711	A3	20061109		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 102004014272	A1	20051020	DE 2004-102004014272	20040322
EP 1727523	A2	20061206	EP 2005-737707	20050317

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU

US 20070184116	A1	20070809	US 2007-593657	20070416

PRIORITY APPLN. INFO.: DE 2004-102004014272A 20040322
WO 2005-EP2884 W 20050317

AB The invention relates to a pharmaceutical formulation containing crystalline and/or amorphous unmilled flutamide that is mixed with at least one surface-active substance. Thus a flutamide capsule included (mg/capsule): unmilled crystalline flutamine 80.0; lactose 70.9; sodium dodecyl sulfate 4.8; microcryst. cellulose 32.0; corn starch 52.0; silica 0.1; magnesium stearate 1.2.

L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:69905 CAPLUS
DOCUMENT NUMBER: 141:169073
TITLE: Development and standardization of a simple binding assay for the detection of compounds with affinity for the androgen receptor
AUTHOR(S): Freyberger, Alexius; Ahr, Hans-Juergen
CORPORATE SOURCE: Bayer AG, Department Molecular and Genetic Toxicology, PH PD P Toxicology, Wuppertal, D-42096, Germany
SOURCE: Toxicology (2004), 195(2-3), 113-126
CODEN: TXCYAC; ISSN: 0300-483X
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Concerns have been raised whether natural and man-made chems. might have the potential of interfering with the endocrine system. Especially interactions with sex hormone receptors are considered as a critical issue. Weak anti-androgenicity has been demonstrated for some environmental pollutants such as p,p'-DDE, and androgenic activity was found in feedlot and pulp mill effluents. To be able to screen for compds. with affinity for the androgen receptor (AR), the authors developed an AR binding assay using a recombinant AR as receptor source and the synthetic androgen methyltrienolone (R 1881) as ligand. Expts. were performed on 96-well microtiter plates. Following method optimization, compds. recently recommended for the validation of assays characterizing AR-mediated

effects and those being used for the OECD validation of the Hershberger assay were employed amongst others to standardize the method. The assay readily detected and discriminated compds. with strong and weak affinity for the AR such as natural and synthetic androgens, anti-androgens in therapeutic use, and a variety of chems. with weak anti-androgenic side effects, whereas in line with previous findings, AR binding properties of dibutylphthalate and its metabolites could not be demonstrated. Detergents interfered with receptor binding, but showed characteristic effects different from that of true AR binding compds. The assay is simple and sensitive, avoids the use of animals as a receptor source, and should be of value when screening for endocrine-modulating compds.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:679428 CAPLUS
DOCUMENT NUMBER: 137:381073
TITLE: The potential of the three-spined stickleback (Gasterosteus aculeatus L.) as a combined biomarker for estrogens and androgens in European waters
AUTHOR(S): Katsiadaki, I.; Scott, A. P.; Mayer, I.
CORPORATE SOURCE: CEFAS Weymouth Laboratory, Dorset, DT4 8UB, UK
SOURCE: Marine Environmental Research (2002), 54(3-5), 725-728
CODEN: MERSDW; ISSN: 0141-1136
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The majority of endocrine disruption studies in Europe have been on non-indigenous species (some of them tropical!)-and none of which has traits that make them suitable for the detection of androgenic compds. To overcome these problems, we have been developing the stickleback as a model biomarker for testing the effect of endocrine disrupters in European waters. Its advantages are: it is the only fish with a quantifiable in vivo androgen and anti-androgen endpoint (the production of the glue protein, spiggin, by the kidney); it is the only fish in which it will be possible to simultaneously test estrogenic and androgenic properties of compound; it has a genetic sex marker; it is found in all EU countries; it survives and breeds in both seawater and freshwater; it is extremely robust and can be readily deployed in situ; it displays a variety of pronounced reproductive behaviors; it has a simple and short life cycle, low fecundity and high egg/fry survival rates.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:672568 CAPLUS
DOCUMENT NUMBER: 131:291309
TITLE: Flutamide compositions and preparations
INVENTOR(S): James, Jack Lawrence; Molnar, Louis Frank, Jr.; Toney-Parker, Tania E.
PATENT ASSIGNEE(S): Applied Analytical Industries, Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952523	A2	19991021	WO 1999-US8111	19990413

WO 9952523 A3 19991202
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6187345 B1 20010213 US 1998-59755 19980414
AU 9935587 A 19991101 AU 1999-35587 19990413
EP 1071415 A2 20010131 EP 1999-917472 19990413
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
US 6228401 B1 20010508 US 2000-685443 20001011
PRIORITY APPLN. INFO.: US 1998-59755 A 19980414
WO 1999-US8111 W 19990413

AB The present invention provides flutamide, having a range of certain particle sizes and sp. surface area, and methods for preparing such flutamide which are useful for preparing pharmaceutical formulations for the treatment of prostatic carcinoma and benign prostatic hypertrophy. Examples are given for milling flutamide with, e.g., lactose, and pharmaceutical formulations are given containing flutamide.

L6 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:766507 CAPLUS
DOCUMENT NUMBER: 130:29221
TITLE: Preparation of solid porous matrixes for pharmaceutical uses
INVENTOR(S): Unger, Evan C.
PATENT ASSIGNEE(S): ImaRx Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851282	A1	19981119	WO 1998-US9570	19980512
W: AU, BR, CA, CN, JP, KR, NZ				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 20020039594	A1	20020404	US 1998-75477	19980511
AU 9873787	A	19981208	AU 1998-73787	19980512
EP 983060	A1	20000308	EP 1998-921109	19980512
R: DE, FR, GB, IT, NL				
US 20010018072	A1	20010830	US 2001-828762	20010409
US 20040091541	A1	20040513	US 2003-622027	20030716

PRIORITY APPLN. INFO.: US 1997-46379P P 19970513
US 1998-75477 A 19980511
WO 1998-US9570 W 19980512
US 2001-828762 B1 20010409

AB A solid porous matrix formed from a surfactant, a solvent, and a bioactive agent is described. Thus, amphotericin nanoparticles were prepared by using ZrO2 beads and a surfactant. The mixture was milled for 24 h.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> D HIS

     (FILE 'HOME' ENTERED AT 08:05:01 ON 01 AUG 2008)

     FILE 'CAPLUS, MEDLINE' ENTERED AT 08:05:38 ON 01 AUG 2008
               E RUNGE HANS-JOACHIM/IN
               E RUNGE HANS/IN
L1           22 S E5
               E LEMBCKE ADALBERT/IN
L2            1 S E3
L3           22 S L1 OR L2
L4         4689 S FLUTAMIDE OR EULEXIN OR FLUTAMIN
L5       177751 S MILL OR MILLING OR UNMILLED OR MILLED
L6            5 S L4 AND L5

=> S L1 NOT L6
L7          21 L1 NOT L6

=> DUPREM L7
DUPREM IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
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"HELP COMMANDS" at an arrow prompt (=>).

=> D L7 1-21 IBIB ABS

L7   ANSWER 1 OF 21  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         1995:397300  CAPLUS
DOCUMENT NUMBER:          122:151390
ORIGINAL REFERENCE NO.:   122:27769a,27772a
TITLE:                    Preparation of 2-hydroxyphenyl-substituted imidazoles
                          as 5-lipoxygenase inhibitors for pharmaceutical use
INVENTOR(S):              Marschner, Frank; Kaestner, Gerd; Kupka, Frank;
                          Luecke, Lothar; Nuhn, Peter; Runge,
                          Hans-Joachim
PATENT ASSIGNEE(S):       Salutas Fahlberg-List Pharma GmbH, Germany
SOURCE:                   Ger. Offen., 6 pp.
                          CODEN: GWXXBX
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     --------------      ----   --------    -------------------    --------
     DE 4320802           A1    19950105    DE 1993-4320802        19930623
PRIORITY APPLN. INFO.:                      DE 1993-4320802        19930623
OTHER SOURCE(S):          CASREACT 122:151390; MARPAT 122:151390
GI
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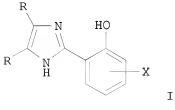

I

AB 2-(2-Hydroxyphenyl)imidazoles I (R = lower alkyl, Ph; or RR completes a benzene ring; X = H, ≥1 alkyl, alkoxy, halo, OH, NO2, CF3, condensed benzene ring) are prepared for use as 5-lipoxygenase inhibitors for treatment of bronchial asthma, inflammatory and allergic disorders, shock, skin diseases (especially psoriasis and polymorphic photodermatosis), cerebral ischemia, and heart infarct, and to prevent transplant rejection. Thus, benzil reacted with 5-chlorosalicylaldehyde in the presence of AcOH/NH4OAc to form 2-(2-hydroxy-5-chlorophenyl)-4,5-diphenylimidazole.

L7 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:397299 CAPLUS
DOCUMENT NUMBER: 122:306557
ORIGINAL REFERENCE NO.: 122:55533a,55536a
TITLE: Preparation of 2-hydroxyphenyl-substituted 1,2,4-triazoles and 1,2,4-oxadiazoles as 5-lipoxygenase inhibitors for pharmaceutical use
INVENTOR(S): Marschner, Frank; Kaestner, Gerd; Kupka, Frank; Luecke, Lothar; Nuhn, Peter; Runge, Hans-Joachim
PATENT ASSIGNEE(S): Salutas Fahlberg-List Pharma GmbH, Germany
SOURCE: Ger. Offen., 6 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4320801	A1	19950105	DE 1993-4320801	19930623
PRIORITY APPLN. INFO.:			DE 1993-4320801	19930623

OTHER SOURCE(S): CASREACT 122:306557; MARPAT 122:306557
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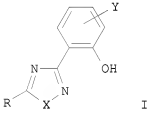


I

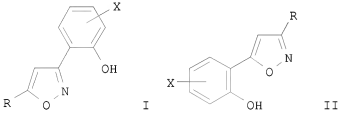
AB 2-(2-Hydroxyphenyl)triazoles and -oxadiazoles I [X = NH, O; R = alkyl, (substituted) Ph, (substituted) naphthyl; Y = H, ≥1 alkyl, alkoxy, halo, OH, NO2, CF3] are prepared for use as 5-lipoxygenase inhibitors for treatment of bronchial asthma, inflammatory and allergic disorders, shock, skin diseases (especially psoriasis and polymorphic photodermatosis), cerebral ischemia, and heart infarct, and to prevent transplant rejection. Thus, benzil reacted with 5-chlorosalicylaldehyde in the presence of AcOH/NH4OAc to form 2-(2-hydroxy-5-chlorophenyl)-4,5-diphenylimidazole.

L7 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:240101 CAPLUS
DOCUMENT NUMBER: 122:178380

ORIGINAL REFERENCE NO.: 122:32461a,32464a
TITLE: 2-Hydroxyphenyl-substituted isoxazole preparation and pharmaceutical use as lipoxygenase and leukotriene hydrolase inhibitors
INVENTOR(S): Marschner, Frank; Kaestner, Gerd; Kupfer, Cornelia; Leucke, Peter; Nuhn, Peter; Runge, Hans-Joachim
PATENT ASSIGNEE(S): Salutas Fahlberg-List Pharma GmbH, Germany
SOURCE: Ger. Offen., 7 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4314966	A1	19941110	DE 1993-4314966	19930506

PRIORITY APPLN. INFO.: DE 1993-4314966 19930506
OTHER SOURCE(S): MARPAT 122:178380
GI

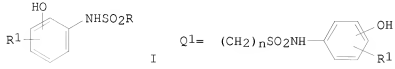


AB Isoxazole derivs. I and II [R = alkyl, (substituted) Ph or naphthyl; X = H, alkyl, alkoxy, halo, OH, NO2, CF3] are prepared as inhibitors of enzymes of the arachidonate cascade for treatment or prophylaxis of bronchial asthma, allergic and inflammatory diseases, shock, psoriasis, cerebral ischemia, transplant rejection, etc. Thus, 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione condensed with NH2OH.HCl to form II (R = Ph; X = H), an inhibitor of LTA4 hydrolase (E.C. 3.3.2.6).

L7 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:457144 CAPLUS
DOCUMENT NUMBER: 121:57144
ORIGINAL REFERENCE NO.: 121:10297a,10300a
TITLE: Preparation of (sulfonylamino)phenols as lipoxygenase and cyclooxygenase inhibitors.
INVENTOR(S): Beger, Joerg; Loose, Sylva; Luecke, Lothar; Neumann, Renate; Runge, Hans Joachim; Schewe, Christiane; Schewe, Tankred
PATENT ASSIGNEE(S): Salutas Fahlberg-List Pharma GmbH, Germany
SOURCE: Ger. Offen., 11 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

DE 4238233 A1 19940519 DE 1992-4238233 19921112
PRIORITY APPLN. INFO.: DE 1992-4238233 19921112
GI

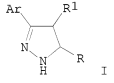


AB Title compds. [I; R = alkyl, cycloalkyl, aralkyl, (substituted) aryl, Q1; R1 = H, alkyl, cycloalkyl, aryl, aralkyl, halo, NO2, CO2H, alkoxycarbonyl; n = 2-14], were prepared Thus, 2-aminophenol in pyridine was treated portionwise with tetradecanesulfonyl chloride and the mixture was kept 5 days to give 56% 2-(tetradecansulfonylamino)phenol. I inhibited 15-lipoxygenase with IC50 = 0.5-44 μM, and inhibited cyclooxygenase with IC50 = 60-1600 μM.

L7 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:408806 CAPLUS
DOCUMENT NUMBER: 119:8806
ORIGINAL REFERENCE NO.: 119:1809a,1812a
TITLE: Preparation and biological activity of 3(5)-(hydroxyaryl)pyrazoles
INVENTOR(S): Kaestner, Gerd; Runge, Hans Joachim; Luecke, Lothar; Loose, Sylva; Schewe, Christiane; Schewe, Tankred
PATENT ASSIGNEE(S): Chemische und Pharmazeutische Fabriken Fahlberg-List G.m.b.H., Germany
SOURCE: Ger. Offen., 9 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4126543	A1	19930211	DE 1991-4126543	19910810

PRIORITY APPLN. INFO.: DE 1991-4126543 19910810
OTHER SOURCE(S): MARPAT 119:8806
GI



AB The preparation of title compds. I (Ar = substituted 2-hydroxyphenyl; R = substituted alkyl, Ph, naphthyl; R1 = H, alkyl, cycloalkyl) as lipoxygenase and cyclooxygenase inhibitors and as well as antiasthmatic bronchodialators, inflammation inhibitors, allergy inhibitors, and skin disease treatment is claimed.

L7 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:235247 CAPLUS
DOCUMENT NUMBER: 116:235247
ORIGINAL REFERENCE NO.: 116:39829a,39832a
TITLE: Process for preparation of α,ω-bis(2-hydroxyphenyl)alkane-α,ω-dione dioximes as lipoxygenase and cyclooxygenase inhibitors
INVENTOR(S): Beger, Joerg; Neumann, Renate; Kaestner, Gerd; Luecke, Lothar; Runge, Hans Joachim; Schewe, Tankred; Schewe, Christiane; Ludwig, Peter; Slapke, Juergen
PATENT ASSIGNEE(S): Chemische und Pharmazeutische Fabriken Fahlberg-List G.m.b.H., Germany
SOURCE: Ger. (East), 5 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 297156	A5	19920102	DD 1990-343504	19900817
DD 297156	B5	19940224		
PRIORITY APPLN. INFO.:			DD 1990-343504	19900817

OTHER SOURCE(S): MARPAT 116:235247
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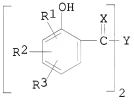


I

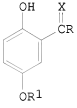
AB The compds. I [R1-R3 = H, alkyl, aralkyl, aryl, alkoxy, aralkoxy, halo, OH; Y = (cyclohexyl or aryl) C2-20 alkylene; X = NOH], useful as lipoxygenase and cyclooxygenase inhibitors, were prepared by oximation of diketones I [X = O, all others as above] with hydroxylamine salts. Thus, 0.24 mol 4-chloro-3-methylphenol was acylated by 0.1 mol sebacic acid dichloride in the presence of AlCl3 to give 1,10-bis(5-chloro-2-hydroxy-4-methylphenyl)decane-1,10-dione. This was treated with H2NOH.HCl to give title compound I [R1 = 5-Cl, R2 = 4-Me, R3 = H, Y = (CH2)8, X = NOH]. A similar I [R1 = 5-OMe, R2 = R3 = H, Y = (CH2)6, X = NOH] had IC50's of 3.8 and 50 μM against lipoxygenase and cyclooxygenase, resp.

L7 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:214145 CAPLUS
DOCUMENT NUMBER: 116:214145
ORIGINAL REFERENCE NO.: 116:36273a,36276a
TITLE: Process for preparation of 2-hydroxyacylphenone oximes as lipoxygenase and cyclooxygenase inhibitors
INVENTOR(S): Beger, Joerg; Neumann, Renate; Vogel, Titus; Luecke, Lothar; Kaestner, Gerd; Runge, Hans Joachim; Schewe, Tankred; Schewe, Christiane; Ludwig, Peter; Slapke, Juergen

PATENT ASSIGNEE(S): Chemische und Pharmazeutische Fabriken Fahlberg-List G.m.b.H., Germany
SOURCE: Ger. (East), 6 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 297155	A5	19920102	DD 1990-343503	19900817

PRIORITY APPLN. INFO.: DD 1990-343503 19900817
OTHER SOURCE(S): MARPAT 116:214145
GI



I

AB Title compds. I [R = alkyl, alkenyl, cycloalkyl, aralkyl, aryl; R1 = H, alkyl, cycloalkyl, aralkyl; X = NOH], useful as lipoxygenase and cyclooxygenase inhibitors, were prepared by oximation of ketones I [X = O, all others as above] with hydroxylamine salts. Thus, p-HOC6H4OH was acylated by octanoyl chloride in the presence of AlCl3 to give 2',5'-dihydroxyoctanophenone. This was treated with H2NOH.HCl to give title compound I [R1 = H, R = n-C7H15, X = NOH] in 80% yield. A similar I [R1 = H, R = n-C13H27, X = NOH] had IC50's of 55 and 24 μM against lipoxygenase and cyclooxygenase, resp.

L7 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:150061 CAPLUS
DOCUMENT NUMBER: 108:150061
ORIGINAL REFERENCE NO.: 108:24621a,24624a
TITLE: Process for preparing 2-[N-methyl-N-(alkoxycarbonylmethyl)sulfamoyl]benzoate esters
INVENTOR(S): Unverferth, Klaus; Laban, Gunter; Guenther, Waltraud; Lohmann, Dieter; Kretzschmar, Egon; Cassebaum, Heinz; Luecke, Lothar; Jassmann, Edgar; Hilger, Herma; Runge, Hans Joachim
PATENT ASSIGNEE(S): VEB Arzneimittelwerk, Ger. Dem. Rep.
SOURCE: Ger. (East), 5 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 247672	A1	19870715	DD 1983-252368	19830627
DD 247672	B1	19890412		

PRIORITY APPLN. INFO.: DD 1983-252368 19830627
OTHER SOURCE(S): CASREACT 108:150061
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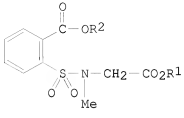

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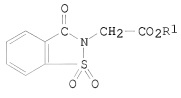

II

AB Title compds. I (R1, R2 = C1-5 alkyl), useful as pharmaceutical intermediates, are prepared from saccharin derivs. II. A MeOH solution containing
1 mol II (R1 = Me) and NaOMe was stirred for .apprx.15 min at 18-25° and then alkylated using (MeO)2SO2 to give 84.7% I (R1 = R2 = Me).

L7 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:131836 CAPLUS
DOCUMENT NUMBER: 108:131836
ORIGINAL REFERENCE NO.: 108:21635a,21638a
TITLE: Preparation of 2-methyl-3-alkoxycarbonyl-4-hydroxy-2H-1,2-benzothiazine-1,1-dioxides as intermediates for inflammation inhibitors
INVENTOR(S): Unverferth, Klaus; Laban, Gunter; Guenther, Waltraud; Lohmann, Dieter; Usbeck, Heinz; Cassebaum, Heinz; Luecke, Lothar; Jassmann, Edgar; Hilger, Herma; Runge, Hans Joachim
PATENT ASSIGNEE(S): VEB Arzneimittelwerk, Ger. Dem. Rep.
SOURCE: Ger. (East), 5 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 247676	A1	19870715	DD 1983-252369	19830627
PRIORITY APPLN. INFO.:			DD 1983-252369	19830627

OTHER SOURCE(S): CASREACT 108:131836
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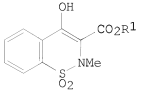


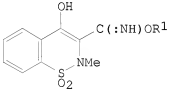
I

AB The title compds. (I; R1 = C1-5 alkyl) were prepared as intermediates for inflammation inhibitors. Me 2-[N-methyl-N-(methoxycarbonylmethyl)sulfamoyl]benzoate was refluxed 2 h with NaOMe in MeOH to give 82.3% I (R1 = Me).

L7 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:598364 CAPLUS
DOCUMENT NUMBER: 107:198364
ORIGINAL REFERENCE NO.: 107:31835a,31838a
TITLE: Preparation of (alkoxycarbimidoyl)hydroxybenzothiazine dioxides as inflammation inhibitors
INVENTOR(S): Unverferth, Klaus; Laban, Gunter; Guenther, Waltraud; Lohmann, Dieter; Kirsten, Wolfgang; Cassebaum, Heinz; Luecke, Lothar; Jassmann, Edgar; Hilger, Herma; Runge, Hans Joachim
PATENT ASSIGNEE(S): VEB Arzneimittelwerk, Ger. Dem. Rep.
SOURCE: Ger. (East), 4 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 245197	A1	19870429	DD 1983-252364	19830627
DD 245197	C2	19871118		
PRIORITY APPLN. INFO.:			DD 1983-252364	19830627

OTHER SOURCE(S): CASREACT 107:198364
GI



I

AB The title compds. (I; R1 = C1-5 alkyl) were prepared as inflammation inhibitors (no data). Mg was refluxed in MeOH to give the alkoxide, 2-methyl-3-cyano-4-hydroxy-2H-1,2-benzothiazine 1,1-dioxide was added, and the mixture was refluxed 1 h to give 81.4% I (R1 = Me).

L7 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1985:560494 CAPLUS
DOCUMENT NUMBER: 103:160494
ORIGINAL REFERENCE NO.: 103:25773a,25776a
TITLE: Saccharin-N-acetic acid esters
INVENTOR(S): Cassebaum, Heinz; Hilger, Herma; Jassmann, Edgar; Luecke, Lothar; Runge, Hans Joachim; Laban, Gunter; Guenther, Waltraud
PATENT ASSIGNEE(S): VEB Fahlberg-List, Ger. Dem. Rep.
SOURCE: Ger. (East), 13 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 215310	A1	19841107	DD 1983-250157	19830425

PRIORITY APPLN. INFO.: DD 1983-250157 19830425

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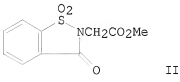

II

AB The title compds. were prepared in high yield and with short reaction times by treating saccharin K or Na salt, optionally prepared in situ, with a haloacetate in a H2O–immiscible solvent with a quaternary ammonium compound phase-transfer catalyst. Thus, saccharin was dissolved in MeOH and neutralized with NaOH. 1,2-Cl2C6H4 was added to the mixture and the MeOH removed by distillation ClCH2CO2Me and a catalytic amount of PhCH2N+Et3Cl- (I) added and the mixture heated 8 h at 95–98° to give 70% II. In the absence of I no II was formed.

L7 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1985:131691 CAPLUS
DOCUMENT NUMBER: 102:131691
ORIGINAL REFERENCE NO.: 102:20655a,20658a
TITLE: N,N'-Bis(3-aroxy-2-hydroxypropyl)alkylenediamines
INVENTOR(S): Runge, Hans Joachim; Luecke, Lothar
PATENT ASSIGNEE(S): VEB Fahlberg-List, Ger. Dem. Rep.
SOURCE: Ger. (East), 8 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 212734	A1	19840822	DD 1982-246653	19821228

PRIORITY APPLN. INFO.: DD 1982-246653 19821228

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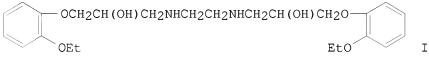

I

AB [ArOCH2CH(OH)CH2NH]2(CH2)n (Ar = aryl; n = 2–6) were prepared Thus, 24.4 g 75% (H2NCH2)2, then 124 g 2-EtOC6H4CH(OH)CH2NH2 were added to 1.0 g PhCH2NEt3Cl in 75 mL 50% KOH, at 386 K, and the mixture was stirred 5 h at 386 K to give 63.8% diamine I.

L7 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1984:551601 CAPLUS

DOCUMENT NUMBER: 101:151601
ORIGINAL REFERENCE NO.: 101:22939a,22942a
TITLE: Technical production of cinnamonitrile
INVENTOR(S): Runge, Hans Joachim; Luecke, Lothar
PATENT ASSIGNEE(S): Ger. Dem. Rep.
SOURCE: Ger. (East), 9 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 208977	A1	19840418	DD 1982-239778	19820512

PRIORITY APPLN. INFO.: DD 1982-239778 19820512

AB PhCH:CHCN(I) was prepared as a cis-trans isomer mixture (mostly trans) by condensation of BzH with MeCN in the presence of < 1 mol highly concentrated (e.g., 50%) aqueous KOH at 328-353K. Thus, 8.48 kg BzH were added over 30 min with cooling to 21.12 L MeCN, 4.48 Kg 50% KOH, and 2.08 kg KOH at .apprx.243K, and the mixture kept 1 h at 238 K to give .apprx. quant. a product containing 83.6 trans-I, 13.8 cis-I, 1.7 PhCH2OH, and 0.9% BzH.

L7 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1984:551571 CAPLUS
DOCUMENT NUMBER: 101:151571
ORIGINAL REFERENCE NO.: 101:22935a,22938a
TITLE: Technical production of triethylbenzylammonium chloride
INVENTOR(S): Runge, Hans Joachim; Luecke, Lothar
PATENT ASSIGNEE(S): Ger. Dem. Rep.
SOURCE: Ger. (East), 8 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 208147	A1	19840328	DD 1981-235879	19811217

PRIORITY APPLN. INFO.: DD 1981-235879 19811217

AB Preparation of PhCH2NEt3Cl (I) from Et3N and PhCH2Cl was improved by using equimolar amts. of reagents in a ketone, especially Me2CO, as solvent. Thus, 20.6 kg PhCH2Cl were added over 1 h at 328 K to 15.35 kg Et3N in 30 L Me2CO, and the mixture was kept 10 h at 328-333 K to give 95% I.

L7 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1981:480741 CAPLUS
DOCUMENT NUMBER: 95:80741
ORIGINAL REFERENCE NO.: 95:13651a,13654a
TITLE: Technical production of orotic acid and its salts
INVENTOR(S): Luecke, Lothar; Runge, Hans Joachim
PATENT ASSIGNEE(S): Ger. Dem. Rep.
SOURCE: Ger. (East), 9 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 144053	A1	19800924	DD 1979-213307	19790531
PRIORITY APPLN. INFO.:			DD 1979-213307	A1 19790531

AB Orotic acid was prepared from maleic anhydride and urea. Thus, 4.9 liquid maleic anhydride was treated with 3 kg urea in AcOH and the product brominated with Br to give 5-bromo-5,6-dihydroorotic acid, which underwent dehydrobromination to give 5.5 orotic acid.

L7 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1981:461814 CAPLUS
DOCUMENT NUMBER: 95:61814
ORIGINAL REFERENCE NO.: 95:10427a,10430a
TITLE: Alkoxy-substituted aminoalkylphenylacetonitrile derivatives
INVENTOR(S): Luecke, Lothar; Runge, Hans Joachim
PATENT ASSIGNEE(S): Ger. Dem. Rep.
SOURCE: Ger. (East), 10 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 144766	A1	19801105	DD 1979-214054	19790703
DD 144766	B1	19870325		
PRIORITY APPLN. INFO.:			DD 1979-214054	A1 19790703

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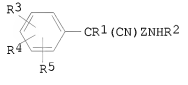

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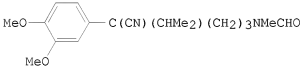

II

AB The title compds. I (R1 = alkyl, cycloalkyl; R2 = alkyl; R3, R4, R5 = H, alkoxy; Z = alkylene) were prepared by treating R3R4R5C6H2CHR1CN with XZNR2R6 (X = halo, R6 = amino protective group) in the presence of phase-transfer catalysts. Treating ground KOH and PhCH2N+Et3Cl- in C6H6 containing 3,4-(MeO)2C6H3CH(CHMe2)CN with HCONMe(CH2)3Cl over 10 min, then refluxing 1 h gave 78% phenylacetonitrile II.

L7 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1981:424593 CAPLUS
DOCUMENT NUMBER: 95:24593
ORIGINAL REFERENCE NO.: 95:4275a,4278a
TITLE: Basic substituted alkoxyphenylacetonitriles
INVENTOR(S): Luecke, Lothar; Runge, Hans Joachim
PATENT ASSIGNEE(S): Ger. Dem. Rep.
SOURCE: Ger. (East), 10 pp.

CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 144052	A1	19800924	DD 1979-213306	19790531
PRIORITY APPLN. INFO.:			DD 1979-213306	A1 19790531

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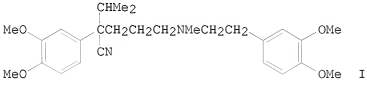


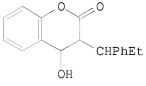
I

AB Manufacture of I without use of alkali amide or hydride was achieved by use of a two-phase system with a phase-transfer catalyst. Thus, 55.4 g 3,4-(MeO)2C6H3CH2NMe(CH2)3Cl in 150 mL THF were added over 10 min to 44 g 3,4-(MeO)2C6H3CH(CHMe2)CN, 1.0 g PhCH2NEt3Cl, and 56 g powdered KOH at reflux, and the mixture was refluxed 40 min to give 91% I.HCl.

L7 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1980:76293 CAPLUS
DOCUMENT NUMBER: 92:76293
ORIGINAL REFERENCE NO.: 92:12563a,12566a
TITLE: 3-(α-Phenylpropyl)-4-hydroxycoumarin
INVENTOR(S): Luecke, Lothar; Runge, Hans Joachim
PATENT ASSIGNEE(S): Ger. Dem. Rep.
SOURCE: Ger. (East), 8 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 136614	A1	19790718	DD 1978-205539	19780524
DD 136614	B1	19841003		
PRIORITY APPLN. INFO.:			DD 1978-205539	A1 19780524

GI



I

AB An improved process for preparing the title compound (I), a known anticoagulant, comprised reaction of the starting materials in

heterogeneous phase in the presence of a mineral or Lewis acid. Yields were improved and side reactions minimized. Thus, 4-hydroxycoumarin suspended in PhMe was treated with 25% H2SO4 and the mixture warmed to 95°. Adding PhCHBrEt over 1.5 h and keeping the mixture a further 3 h at 95° gave 81.5% crude I.

L7 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1978:89350 CAPLUS
DOCUMENT NUMBER: 88:89350
ORIGINAL REFERENCE NO.: 88:13995a,13998a
TITLE: 1-Substituted 1-phenyl-1-hydroxy-3-aminopropanes
INVENTOR(S): Luecke, Lothar; Runge, Hans Joachim
PATENT ASSIGNEE(S): Ger. Dem. Rep.
SOURCE: Ger. (East), 12 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 124521	A1	19770302	DD 1976-191862	19760316
PRIORITY APPLN. INFO.:			DD 1976-191862	A1 19760316

AB HOCRPhCH2CH2R1 (R = cyclohexyl or Et, R1 = morpholino; R = cyclohexyl, Me2CH, nortricyclenyl, R1 = piperidino) were prepared in 76-88% yield by the Grignard reaction of RX (X = Br or Cl) with PhCOCH2CH2R1. HOCEtPhCHMeCH2R1 (R1 = piperidino) was similarly prepared from EtBr and PhCOCHMeCH2R1.

L7 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1977:534458 CAPLUS
DOCUMENT NUMBER: 87:134458
ORIGINAL REFERENCE NO.: 87:21357a,21360a
TITLE: Substituted phenylethylamine derivatives
INVENTOR(S): Runge, Hans Joachim; Luecke, Lothar; Loew, Hannelore; Brueckner, Roland
PATENT ASSIGNEE(S): Ger. Dem. Rep.
SOURCE: Ger. (East), 36 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 122967	A1	19761112	DD 1975-187214	19750710
PRIORITY APPLN. INFO.:			DD 1975-187214	19750710

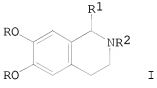
AB Fifty-eight 3,4-(RO)2C6H3CH2CH2NR1R2 [I; R = H or Me; R1 = H, alkyl, or aralkyl; R2 = H, CH[(CH2)mR3](CH2)nR4 (R3 = Ph, substituted phenyl, etc., R4 = H or Ph, m and n = the same or different whole nos. 0-3), ω-benzoylalkyl or a ring-substituted derivative, or CH2CH(OH)CH2OR5 (R5 = Ph or alkoxy- or allyl-substituted phenyl)] were prepared as the free base, hydrochloride, or oxalate. Thus, a mixture of CO[(CH2)3Ph]2 with 3,4-(MeO)2C6H3CH2CH2NH2 was hydrogenated over PtO2 at normal pressure to give 81.5% I.HCl [R = Me, R1 = H, R2 = CH[(CH2)3Ph]2]. I are hypotensives, antiarrhythmic agents, and coronary dilators (no data).

L7 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1977:453109 CAPLUS

DOCUMENT NUMBER: 87:53109
ORIGINAL REFERENCE NO.: 87:8415a,8418a
TITLE: Pharmacologically active tetrahydroisoquinolines
INVENTOR(S): Luecke, Lothar; Runge, Hans Joachim; Brueckner, Roland; Loew, Hannelore
PATENT ASSIGNEE(S): Ger. Dem. Rep.
SOURCE: Ger. (East), 6 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 121321	A1	19760720	DD 1975-185660	19750424
PRIORITY APPLN. INFO.:			DD 1975-185660	A1 19750424

GI



I

AB I [R = H, Me; R1 = H, Ph2CHCH2; R2 = H, (PhCH2CH2)2CH, PhCH2CHPh, 4-MeC6H4CH2, 2,3-(HO)(MeO)C6H3CH2, (PhCH2CH2CH2)2CH, PhCH2CHEt, 4-HOC6H4CH2], useful as antiarrhythmics and vasodilators (no data), are prepared by known procedures. Thus, reaction of 3,4-(MeO)2C6H3CH2CH2NH2 with Ph2C:CHCHO in C6H6 gives after 1 h reflux 92.5% 3,4-(MeO)2C6H3CH2CH2N:CHCH:CPh2 (II). Cyclization of II in 24% aqueous HCl at 100° gives after 5 h 78% I.C2H2O4 (R = Me, R1 = Ph2C:CH, R2 = H) (III). Hydrogenation of III free base in MeOH over PtO2 at 25°/1 atm gives 81% I.HCl (R = Me, R1 = Ph2CHCH2, R2 = H).

=> D HIS

(FILE 'HOME' ENTERED AT 08:05:01 ON 01 AUG 2008)

FILE 'CAPLUS, MEDLINE' ENTERED AT 08:05:38 ON 01 AUG 2008
E RUNGE HANS-JOACHIM/IN
E RUNGE HANS/IN
L1 22 S E5
E LEMBCKE ADALBERT/IN
L2 1 S E3
L3 22 S L1 OR L2
L4 4689 S FLUTAMIDE OR EULEXIN OR FLUTAMIN
L5 177751 S MILL OR MILLING OR UNMILLED OR MILLED
L6 5 S L4 AND L5
L7 21 S L1 NOT L6

=> S UNMILLED (10A) L4
L8 1 UNMILLED (10A) L4

=> S PHARMACEUTICAL
L9 461227 PHARMACEUTICAL

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=> S UNMILLED
L10         507 UNMILLED

=> S L9 AND L10
L11          27 L9 AND L10

=> S L11 NOT L6
L12          26 L11 NOT L6

=> S L9 (20A) L10
L13           2 L9 (20A) L10

=> D L13 1-2 IBIB ABS

L13  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2006:321980  CAPLUS
DOCUMENT NUMBER:          144:376461
TITLE:                    Isomorphic crystalline habits of 3α-hydroxy-21-
                          (1-imidazolyl)-3β-methoxymethyl-5α-pregnan-
                          20-one
INVENTOR(S):              Goliber, Philip A.; Leary, Pauline E.; Danagher,
                          Helen; Hartenstein, Matthew
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 18 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ---------------     ----   --------    --------------------    --------
     US 20060074059       A1    20060406    US 2005-211784          20050825
PRIORITY APPLN. INFO.:                      US 2004-604447P     P   20040826
GI
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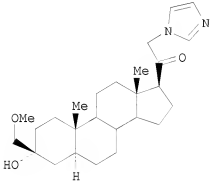

I

AB The present invention provides stable particles of the title compound (I), which possess and retain a shape and size appropriate for handling and manufacture of large-scale pharmaceutical prepns., even in the absence of further milling. Further provided is a method for obtaining such reproducible, stable particles by subjecting crude I to controlled crystallization conditions comprising slow cooling of a solution of I. Further provided is a

pharmaceutical composition of unmilled crystalline I, which does not require milling prior to formulation, and a method of modulating brain excitability using the same.

L13 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1042029 CAPLUS
DOCUMENT NUMBER: 143:312056
TITLE: Pharmaceutical formulation containing unmilled flutamide
INVENTOR(S): Runge, Hans-Joachim; Lembcke, Adalbert
PATENT ASSIGNEE(S): Hexal A.-G., Germany
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005089711	A2	20050929	WO 2005-EP2884	20050317
WO 2005089711	A3	20061109		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 102004014272	A1	20051020	DE 2004-102004014272	20040322
EP 1727523	A2	20061206	EP 2005-737707	20050317
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
US 20070184116	A1	20070809	US 2007-593657	20070416
PRIORITY APPLN. INFO.:			DE 2004-102004014272A	20040322
			WO 2005-EP2884 W	20050317

AB The invention relates to a pharmaceutical formulation containing crystalline and/or amorphous unmilled flutamide that is mixed with at least one surface-active substance. Thus a flutamide capsule included (mg/capsule): unmilled crystalline flutamine 80.0; lactose 70.9; sodium dodecyl sulfate 4.8; microcryst. cellulose 32.0; corn starch 52.0; silica 0.1; magnesium stearate 1.2.

=> S L12 NOT L13
L14 25 L12 NOT L13

=> D L14 1-25 IBIB ABS

L14 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:601323 CAPLUS
DOCUMENT NUMBER: 149:95389
TITLE: Oral delivery of 1,3-dicyclohexylurea nanosuspension enhances exposure and lowers blood pressure in hypertensive rats
AUTHOR(S): Ghosh, Sarbani; Chiang, Po-Chang; Wahlstrom, Jan L.;

	Fujiwara, Hideji; Selbo, Jon G.; Roberds, Steven L.
CORPORATE SOURCE:	Pfizer Global Research and Development, St. Louis Laboratories, Pfizer Inc., Chesterfield, MO, USA
SOURCE:	Basic & Clinical Pharmacology & Toxicology (2008), 102(5), 453-458 CODEN: BCPTBO; ISSN: 1742-7835
PUBLISHER:	Blackwell Publishing Ltd.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Cytochrome P 450-derived epoxyeicosatrienoic acids (EET) are biol. active metabolites of arachidonic acid that have potent effects on renal vascular reactivity and tubular ion transport and have been implicated in the control of blood pressure. EETs are hydrolyzed to their less active diols, dihydroxyeicosatrienoic acids (DHET), by the enzyme soluble epoxide hydrolase (sEH). 1,3-Dicyclohexylurea (DCU), a potent sEH inhibitor, lowers systemic blood pressure in spontaneously hypertensive rats when dosed i.p. However, DCU has poor aqueous solubility, posing a challenge for in vivo oral delivery. To overcome this limitation, we formulated DCU in a nanosuspension using wet milling. Milling reduced particle size, increasing the total surface area by approx. 40-fold. In rats chronically infused with angiotensin II, the DCU nanosuspension administered orally twice daily for 4 days produced plasma exposures an order of magnitude greater than unmilled DCU and lowered blood pressure by nearly 30 mmHg. Consistent with the mechanism of sEH inhibition, DCU increased plasma 14,15-EET and decreased plasma 14,15-DHET levels. These data confirm the antihypertensive effect of sEH inhibition and demonstrate that greatly enhanced exposure of a low-solubility compound is achievable by oral delivery using a nanoparticle drug delivery system.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2008:555007 CAPLUS
DOCUMENT NUMBER:	148:592669
TITLE:	The use of atomic force microscopy to study the conditioning of micronized budesonide
AUTHOR(S):	Jones, Matthew D.; Young, Paul M.; Traini, Daniela; Shur, Jagdeep; Edge, Stephen; Price, Robert
CORPORATE SOURCE:	Pharmaceutical Surface Science Research Group, Department of Pharmacy & Pharmacology, University of Bath, Bath, BA2 7AY, UK
SOURCE:	International Journal of Pharmaceutics (2008), 357(1-2), 314-317 CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER:	Elsevier B.V.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Patent literature describes "conditioning" techniques which employ organic vapors to recrystallize amorphous regions in micronized particles, with the aim of improving their processability and physico-chemical stability. This report describes a preliminary study investigating the efficacy of PhaseImaging atomic force microscopy (AFM) for the investigation of such processes. AFM phase images demonstrated variation in mech. properties across the surface of milled budesonide particles, which diminished upon exposure to ethanol vapor. No variation was seen in phase images of unmilled budesonide. Dynamic vapor sorption confirmed the presence amorphous material in the milled sample and its subsequent recrystn. following exposure to ethanol vapor under the same conditions as those used in the AFM experiment It was therefore hypothesised that variation in the phase images indicated the presence of amorphous regions which were subsequently conditioned. PhaseImaging AFM may therefore be a useful

method for the study of conditioning techniques, enabling the efficacy and kinetics of the process to be observed
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:902156 CAPLUS
DOCUMENT NUMBER: 141:355408
TITLE: Stabilized prostaglandin formulation
INVENTOR(S): Burgess, George Alexander; Douglas, Scott L.; Heimlich, John Mark; Miller, Jim F.; Rohrs, Brian Robert
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091579	A1	20041028	WO 2004-IB1199	20040405
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20050031690	A1	20050210	US 2004-825397	20040415
PRIORITY APPLN. INFO.:			US 2003-463356P P	20030416

AB A discrete solid orally deliverable pharmaceutical dosage form, e.g., a capsule or tablet, comprises (a) at least one first zone containing an NSAID, and (b) at least one second zone containing HPMC having dispersed therein a prostaglandin type compound in a form of a substantially water-free solid dispersion. The zones are spatially arranged such that, if there is only one first zone and one second zone, these zones are arranged other than as a core and mantle, resp., separated by an enteric coating layer. The HPMC comprises a fraction having particle size smaller than about 53 μm exhibiting, upon dissoln. in CO2-free purified water to form a 1% weight/volume solution, a pH not lower than about 4. An assay method is also provided for selecting suitable lots of HPMC for use in preparing such a dosage form. For example, a dispersion of 1 part misoprostol in 99 parts HPMC was prepared using HPMC of milled and unmilled samples. The unmilled HPMC, having a high degree of residual acidity, as indicated by a pH of the sub-53 μm fraction that was lower than 4, provided a dispersion exhibiting poor misoprostol stability. The same lot after milling was found to have low residual acidity and provided a dispersion having acceptable misoprostol stability.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:517554 CAPLUS
DOCUMENT NUMBER: 121:117554

ORIGINAL REFERENCE NO.: 121:21057a,21060a
TITLE: Dicalcium phosphate dihydrate for direct compression: Characterization and intermanufacturer variability
AUTHOR(S): Landin, M.; Martinez-Pacheco, R.; Gomez-Amoza, J. L.; Souto, C.; Concheiro, A.; Rowe, R. C.
CORPORATE SOURCE: Departamento de Farmacologia, Farmacia y Tecnologia Farmaceutica, Facultad de Farmacia, Universidad de Santiago, Santiago de Compostela, 15706, Spain
SOURCE: International Journal of Pharmaceutics (1994), 109(1), 1-8
CODEN: IJPHDE; ISSN: 0378-5173
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The structure, dehydration behavior, and particle characteristics of the 2 currently available com. brands of unmilled dicalcium phosphate dihydrate (DCPD) for direct compression, Emcompress and DiTab, were studied. The 2 brands have very similar properties, differing significantly only in intraparticle porosity. As a consequence, their compression and flow properties are effectively identical. The characteristics of Emcompress and Ditab were compared with those of 2 DCPD powders, Calipharm (whose properties are typical of milled DCPD prepns.) and Kyowa (whose properties are in many respects atypical). The processing undergone by unmilled DCPD for direct compression does not cause major changes in crystal structure, mech. and surface properties with respect to typical powders. However, there are considerable differences in dehydration behavior, which can probably be attributed to the larger mean particle size and different particle structure of the direct compression prepns.

L14 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:491638 CAPLUS
DOCUMENT NUMBER: 121:91638
ORIGINAL REFERENCE NO.: 121:16315a,16318a
TITLE: Surface morphology study of solid powders evaluated by particle size distribution and nitrogen adsorption
AUTHOR(S): Faroongsarng, Damrongsak; Peck, Garnet E.
CORPORATE SOURCE: School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, IN, 47907, USA
SOURCE: Drug Development and Industrial Pharmacy (1994), 20(15), 2353-67
CODEN: DDIPD8; ISSN: 0363-9045
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The surface morphol. of five tableting excipients including unmilled dicalcium phosphate dihydrate (Di-Tab), microcryst. cellulose (Avicel PH102), corn starch, croscarmellose sodium (Ac-di-sol), and sodium starch glycolate (Primojel) was studied using laser scattering particle size anal. and nitrogen adsorption surface area anal. The surface area of particles disregarding porosity was obtained from the particle size distribution and the total area was obtained from the B.E.T. treatment of nitrogen adsorption results. The so-called Surface Irregularity Index (SII) was established to indicate surface roughness due to porosity. The SII value was consistent with the microscopic visualization of a powder sample. Furthermore, the nitrogen adsorption-desorption isotherm hysteresis which showed the evidence of porosity was also consistent with the index. The SII may be an alternative way to characterize the surface morphol. of a solid powder.

L14 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:417854 CAPLUS
DOCUMENT NUMBER: 121:17854

ORIGINAL REFERENCE NO.: 121:3287a,3290a
TITLE: The role of liquid water uptake by an insoluble tablet containing a disintegrant
AUTHOR(S): Faroongsarng, Damrongsak; Peck, Garnet E.
CORPORATE SOURCE: Sch. Pharm. Pharmacal Sci., Purdue Univ., West Lafayette, IN, 47907, USA
SOURCE: Drug Development and Industrial Pharmacy (1994), 20(10), 1777-94
CODEN: DDIPD8; ISSN: 0363-9045
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The hydration capacity of each of 4 disintegrants including microcryst. cellulose (Avicel PH102), corn starch, croscarmellose sodium (Ac-di-sol) and sodium starch glycolate (Primojel) was determined to express the hydrophilicity. The complete pore structure, and the water uptake of unmilled dicalcium phosphate dihydrate (D-Tab) tablets containing one of above disintegrants at 15% level were studied. The majority of the tablet porosity was made up by macropores which were accessed by mercury intrusion. There was no statistically significant difference among pore volume-size distributions of tablet samples. The water uptake results were treated by the empirical form of Washburn liquid penetration equation with appropriate exptl. setup. It was possible to determine the significance of the empirical parameters drawn from the equation. The hydrophilic nature of excipients present in a tablet played a major role in water uptake phenomenon. It is suggested that the disintegrant swelling narrows the pore sizes in the beginning and then the pores widen due to the repelling pressure exerted causing the tablets to collapse. Finally, the water penetration is impeded by gelling formation of a disintegrant present in a tablet matrix.

L14 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:143996 CAPLUS
DOCUMENT NUMBER: 120:143996
ORIGINAL REFERENCE NO.: 120:25195a,25198a
TITLE: Factorial design of phenylpropanolamine prolonged-release tablet formulations using fluid-bed dryer granulator
AUTHOR(S): Mesiha, Mounir S.; Rivera, Daisy
CORPORATE SOURCE: Arnold and Marie Schwartz Coll. Pharm., Long Island Univ., Brooklyn, NY, 11201, USA
SOURCE: Drug Development and Industrial Pharmacy (1994), 20(1), 31-48
CODEN: DDIPD8; ISSN: 0363-9045
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A two level factorial design approach was applied to the formulation of prolonged-release phenylpropanolamine tablets using three factors: Et acrylate-Me methacrylate copolymer (Eudragit NE-40D) concentration, microcryst. cellulose (Avicel PH102) addition to the tablets formula, and the milling of the granulations before compression. The release rate of the drug was the measured parameter. The rate of drug release was mainly affected by the level of the Eudragit. Avicel promotes the release of the drug, specially at low Eudragit level concns. Tablets prepared from unmilled lots showed slower drug release than the corresponding lots of milled granules.

L14 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:62166 CAPLUS
DOCUMENT NUMBER: 120:62166
ORIGINAL REFERENCE NO.: 120:11109a,11112a
TITLE: Effects of particle size of bulk drug and food on the bioavailability of U-78875 in dogs

AUTHOR(S): Nishihata, Toshiaki; Ishizaka, Mayumi; Yokohama, Sigeharu; Martino, Alice C.; Gordon, Roger E.
CORPORATE SOURCE: Tsukuba Res., Upjohn Pharm. Ltd., Tsukuba, 300-42, Japan
SOURCE: Drug Development and Industrial Pharmacy (1993), 19(20), 2679-98
CODEN: DDIPD8; ISSN: 0363-9045
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of particle size and food on the absolute bioavailability of U-78875 in dogs after oral administration of either a suspension or tablet dosage form were investigated. A reduction of particle size caused a significant increase in bioavailability along with an increase in dissoln. rate. Addnl., both suspension and tablet dosage forms administered after food caused an increase in bioavailability. Thus, to accelerate drug dissoln., a reduction of U-78875 particle size from the unmilled state is important for the optimization of formulation compns. To increase the bioavailability of U-78875, postprandial dosing should be considered.

L14 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:66717 CAPLUS
DOCUMENT NUMBER: 118:66717
ORIGINAL REFERENCE NO.: 118:11705a,11708a
TITLE: Physical and lubrication properties of magnesium stearate
AUTHOR(S): Leinonen, U. I.; Jalonen, H. U.; Vihervaara, P. A.; Laine, E. S. U.
CORPORATE SOURCE: Orion Corp., Turku, SF-20101, Finland
SOURCE: Journal of Pharmaceutical Sciences (1992), 81(12), 1194-8
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The lubrication properties of 2 com.-grade magnesium stearates were studied. Their moisture contents and crystal structures were similar. There were minor differences in their fatty acid composition, but the differences did not affect the lubrication properties. The lubrication properties correlated with particle size distributions and sp. surface area. The effect of these parameters was further studied with unmilled and milled chemical pure magnesium stearate. Milling decreased the particle size and increased the sp. surface area. In both cases, the batch with a smaller particle size and larger sp. surface area had considerably better lubricity.

L14 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:433682 CAPLUS
DOCUMENT NUMBER: 117:33682
ORIGINAL REFERENCE NO.: 117:5899a,5902a
TITLE: Coated delivery system for cyclic amino acids with improved taste, texture and compressibility
INVENTOR(S): Cherukuri, Subraman Rao; Chau, Tommy Linkwong
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 458751	A1	19911127	EP 1991-810380	19910517
R: BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE				
JP 04270216	A	19920925	JP 1991-148198	19910524
PRIORITY APPLN. INFO.:			US 1990-530768	A 19900525

OTHER SOURCE(S): MARPAT 117:33682

AB A core made of a cyclic amino acid (Markush given), such as the drug Gabapentin is first coated with a water-soluble or water-insol. polymeric film and then with a hydrophilic coating made of fats, fatty acids and/or waves. Unmilled Gabapentin was granulated with excipients and coated with gelatin type A and then with a mixture of partially-hydrogenated soybean oil and glycerol monostearate.

L14 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:226748 CAPLUS
DOCUMENT NUMBER: 108:226748
ORIGINAL REFERENCE NO.: 108:37129a,37132a
TITLE: Studies on direct compression of tablets. XIX. The effect of particle size and shape on the mechanical strength of sodium bicarbonate tablets
AUTHOR(S): Alderborn, G.; Borjesson, E.; Glazer, M.; Nystrom, C.
CORPORATE SOURCE: Uppsala Biomed. Cent., Uppsala Univ., Uppsala, S-751 23, Swed.
SOURCE: Acta Pharmaceutica Suecica (1988), 25(1), 31-40
CODEN: APSXAS; ISSN: 0001-6675
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Five size fractions of crystalline NaHCO3, a material which reduces in volume mainly by plastic deformation, were prepared by dry sieving. For one of the size fractions, 90-125 μm, both a milled and an unmilled fraction was prepared All powders were examined by microscopy and then compressed in an instrumented single punch press at 2 pressures (200 and 300 MPa). Finally, the radial and the axial tensile strength of the tablets were measured. From these data the strength isotropy ratio was also calculated Porosity changes during compression at 150 MPa were also registered and plotted according to the Heckel function. Both the radial and the axial tensile strengths and the values for the strength isotropy ratio were fairly constant over the particle size range studied. For the 90-125 μm fraction, the milled quality gave a significantly higher tablet strength than the unmilled. Even the strength isotropy ratio was higher for the milled quality. The volume reduction behavior, as evaluated by the Heckel plots, was similar for the unmilled and milled quality of the 90-125 μm fraction.

L14 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:605152 CAPLUS
DOCUMENT NUMBER: 107:205152
ORIGINAL REFERENCE NO.: 107:32839a,32842a
TITLE: Extrusion of an effervescent granulation with a twin screw extruder, Baker Perkins MPF 50 D
AUTHOR(S): Lindberg, N. O.; Tufvesson, C.; Olbjer, L.
CORPORATE SOURCE: AB Leo, Helsingborg, S-251 09, Swed.
SOURCE: Drug Development and Industrial Pharmacy (1987), 13(9-11), 1891-913
CODEN: DDIPD8; ISSN: 0363-9045
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Anhydrous citric acid and NaHCO3 were granulated with EtOH in an extruder. The load on the motor, the dwell time, the fraction above 1.00 mm and below 0.125 mm of unmilled granulation, the geometric mean diameter by weight and the CO2 content of the milled granulation were influenced by

all these process variables: powder flow rate, EtOH concentration, screw speed, die restriction and screw configuration. However, the impact of powder flow rate, EtOH concentration and screw speed was partly of an interaction type, except in the case of motorload. As the response variables showed significant interactions, the dependence on the process variables was complex. The temperature of the extrudate was affected by screw configuration, die plate and EtOH concentration without any interactions. Regarding the output, this variable was influenced by screw configuration and by an interaction between EtOH concentration and die plate.

L14 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1975:415582 CAPLUS
DOCUMENT NUMBER: 83:15582
ORIGINAL REFERENCE NO.: 83:2525a,2528a
TITLE: Effect of particle size upon mixture homogeneity
AUTHOR(S): Johnson, M. C. R.
CORPORATE SOURCE: Pharm. Dev., Ciba-Geigy Ltd., Basel, Switz.
SOURCE: Pharmaceutica Acta Helvetiae (1975), 50(3), 60-3
CODEN: PAHEAA; ISSN: 0031-6865
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Excipient type did not influence mixture homogeneity of 1% unmilled cyclopenthiazide [742-20-1] (mean particle size 50 μm) mixed in a Turbula mixer for 20 min at 50 rpm. However, using 1% milled drug (mean particle size 22 μm), a segregation effect was observed with both coarse and fine lactose [63-42-3] after 20 min of mixing. The mixts. containing the other excipients were all homogeneous. Thus, drug particle size distribution controls the coefficient of variation of the mixture at this concentration

L14 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1974:112584 CAPLUS
DOCUMENT NUMBER: 80:112584
ORIGINAL REFERENCE NO.: 80:18079a,18082a
TITLE: Influence of excipient type and drug particle size upon a small-scale mixing process
AUTHOR(S): Johnson, M. C. R.
CORPORATE SOURCE: Pharm. Dev., Ciba-Geigy Ltd., Basel, Switz.
SOURCE: Journal of Pharmacy and Pharmacology (1973), 25(Suppl.), 162P-163P
CODEN: JPPMAB; ISSN: 0022-3573
DOCUMENT TYPE: Journal
LANGUAGE: English
AB With unmilled cyclopenthiazide (I) the choice of excipient did not effect the quality of the final mixture, but with milled I instability and segregation of mixts. could be avoided by using wheat or maize starch in place of lactose. Experiment coeffs. of variation were determined by the particle size of I. the values for 1% weight mixts. of milled and unmilled I, which had mean particle sizes of 22 μm resp., being 0.7 and 3.0 resp.

L14 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1973:62154 CAPLUS
DOCUMENT NUMBER: 78:62154
ORIGINAL REFERENCE NO.: 78:9829a,9832a
TITLE: Design and use of a laboratory extruder for pharmaceutical granulations
AUTHOR(S): Goodhart, Frank W.; Draper, J. Ronald; Ninger, Fred C.
CORPORATE SOURCE: Div. Pharm. Res. Dev., Warner-Lambert Res. Inst.,

Morris Plains, NJ, USA
SOURCE: Journal of Pharmaceutical Sciences (1973), 62(1), 133-6
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A laboratory extruder was designed and built and factors relating to its use for the preparation of both wet and hot fusion granulations were evaluated. The extruder used was a specially designed, single screw type, equipped with removable anvils, liquid addition ports, a heating jacket, and a thermocouple probe. A study of the extrusion of a typical antacid granulation was made. The variables studied were: (a) type of granulating fluid, (b) type of endplate, (c) number of mixing anvils, and (d) screw speed. Measurements were made on torque, powder throughput, liquid required, and whether or not a uniform consistency was obtained. Mesh sizes of both milled and unmilled granulation were measured along with bulk ds. of 30-40-mesh fractions. A series of wax fusion granulations was also made with varying jacket temps., and drug release rates for 1 and 5 hr were tested.

L14 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1969:31657 CAPLUS
DOCUMENT NUMBER: 70:31657
ORIGINAL REFERENCE NO.: 70:5953a,5956a
TITLE: Interdependence of physiological surfactant and drug particle size on the dissolution behavior of water-insoluble drugs
AUTHOR(S): Lin, Song-Ling; Menig, Johanne; Lachman, Leon
CORPORATE SOURCE: Develop. and Contr. Dep., Ciba Pharm. Co., Summit, NJ, USA
SOURCE: Journal of Pharmaceutical Sciences (1968), 57(12), 2143-8
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of in vitro expts. was performed to demonstrate the interdependence of physiologic surfactant and drug particle size on the dissoln. rate of glutethimide, griseofulvin, and a new diuretic Compound A. The presence of physiol. concns. of lysolecithin (a naturally occurring biosurfactant) is shown to exhibit micellar solubilizing properties on the drugs investigated. The data obtained from the dissoln. rate studies showed that aqueous lysolecithin solution caused significant enhancement of the extent of solution of the drugs investigated. However, the reduction of particle size through micronization may not necessarily increase the in vitro dissoln. rate. Data to support this statement are presented, and a plausible explanation for its occurrence is the electrostatic charge that develops on the solids after milling. This results in aggregates which can be larger in particle size than the unmilled drug.

L14 ANSWER 17 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2007033955 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17233537
TITLE: Anisotropic surface chemistry of crystalline pharmaceutical solids.
AUTHOR: Heng Jerry Y Y; Bismarck Alexander; Williams Daryl R
CORPORATE SOURCE: Imperial College London, Department of Chemical Engineering, South Kensington Campus, London SW7 2AZ, United Kingdom.
SOURCE: AAPS PharmSciTech, (2006) Vol. 7, No. 4, pp. 84.

Electronic Publication: 2006-10-06.
Journal code: 100960111. E-ISSN: 1530-9932.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200702
ENTRY DATE: Entered STN: 20 Jan 2007
Last Updated on STN: 1 Mar 2007
Entered Medline: 28 Feb 2007

AB The purpose of this study was to establish the link between the wetting behavior of crystalline pharmaceutical solids and the localized surface chemistry. A range of conventional wetting techniques were evaluated and compared with a novel experimental approach: sessile drop contact angle measurements on the individual facets of macroscopic (>1 cm) single crystals. Conventional measurement techniques for determining surface energetics such as capillary rise and sessile drops on powder compacts were found not to provide reliable results. When the macroscopic crystal approach was used, major differences for advancing contact angles, theta(a), of water were observed-as low as 16 degrees on facet (001) and as high as 68 degrees on facet (010) of form I paracetamol. theta(a) trends were in excellent agreement with X-ray photoelectron spectroscopy surface composition and known crystallographic structures, suggesting a direct relationship to the local surface chemistry. Inverse gas chromatography (IGC) was further used to probe the surface properties of milled and unmilled samples, as a function of particle size. IGC experiments confirmed that milling exposes the weakest attachment energy facet, with increasing dominance as particle size is reduced. The weakest attachment energy facet was also found to exhibit the highest theta(a) for water and to be the most hydrophobic facet. This anisotropic wetting behavior was established for a range of crystalline systems: paracetamol polymorphs, aspirin, and ibuprofen racemates. theta(a) was found to be very sensitive to the local surface chemistry. It is proposed that the hydrophilicity/hydrophobicity of facets reflects the presence of functional groups at surfaces to form hydrogen bonds with external molecules.

L14 ANSWER 18 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2006305295 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16527466
TITLE: Water retention and drainage in different brands of microcrystalline cellulose: effect of measuring conditions.
AUTHOR: Nikolakakis Ioannis; Tsarvouli Konstantina; Malamataris Stavros
CORPORATE SOURCE: Department of Pharmaceutical Technology, School of Pharmacy, Aristotle University of Thessaloniki, Thessaloniki, Greece.
SOURCE: European journal of pharmaceutics and biopharmaceutics : official journal of Arbeitsgemeinschaft fur Pharmazeutische Verfahrenstechnik e.V, (2006 Jul) Vol. 63, No. 3, pp. 278-87. Electronic Publication: 2006-03-09.
Journal code: 9109778. ISSN: 0939-6411.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 31 May 2006
Last Updated on STN: 27 Oct 2006
Entered Medline: 26 Oct 2006

AB Interaction between water and microcrystalline cellulose (MCC) measured as retention and cumulative drainage of water (WR% and CDW%) is investigated for unmilled and micronized standard (Avicel and Emcocel) and silicified (Prosolv) MCC brands. A centrifuge method was applied with increasing duration and different porosity and thickness of cylindrical powder beds (specimens), in order to establish optimal determination conditions and quantify alterations in interaction between water and different MCC brands. Also, changes of specimen thickness due to presence of water (swelling) were followed. It was found that the effect of specimen porosity and thickness on water drainage (CDW%) appears to be opposite to that on water retention (WR%), while two patterns of WR% and CDW% change with specimen porosity and thickness can be distinguished depending on the centrifugation time. Also, WR% and CDW% are affected by the MCC brand and the micronization. Unmilled silicified MCC brand (Prosolv) shows significantly lower retention and higher drainage of water compared to standard unmilled brands (Avicel and Emcocel), while differences between the unmilled standard Avicel and Emcocel brands are not easily distinguished. Micronization, in general, increases greatly the WR% and decreases CDW% for all the tested MCC brands, and enhances their differences even between Avicel and Emcocel. Swelling of specimen due to presence of water was observed, which was significantly reduced with the micronization, the specimen porosity, and centrifugation as well, but showed slight variation between the different MCC brands. Values of specimen porosity between 60% and 70%, thickness/diameter ratio between 0.75 and 1.0, and centrifugation time between 5 and 20 min provide optimal measuring settings for comparison of MCC brands.

L14 ANSWER 19 OF 25 MEDLINE on STN

ACCESSION NUMBER:	2006146217 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 16382277
TITLE:	A study on the effect of wet granulation on microcrystalline cellulose particle structure and performance.
AUTHOR:	Badawy Sherif I Farag; Gray David B; Hussain Munir A
CORPORATE SOURCE:	Pharmaceutical Research Institute, Bristol-Myers Squibb Co., One Squibb Drive, New Brunswick, New Jersey, 08903, USA.. sherif.badawy@bms.com
SOURCE:	Pharmaceutical research, (2006 Mar) Vol. 23, No. 3, pp. 634-40. Electronic Publication: 2006-01-01. Journal code: 8406521. ISSN: 0724-8741.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200701
ENTRY DATE:	Entered STN: 15 Mar 2006 Last Updated on STN: 12 Jan 2007 Entered Medline: 11 Jan 2007

AB PURPOSE: The aim of this study was to investigate the mechanism of the effect of wet granulation process on the compaction properties of microcrystalline cellulose (MCC). METHODS: MCC alone and with hydroxypropyl cellulose (HPC) as a binder were wet granulated by a high-shear process using different granulation parameters (over- and undergranulated). Overgranulated batches were also ball milled after drying and compared to the unmilled material. MCC starting material and granulation were characterized for particle size distribution, surface area, porosity, and isothermal moisture uptake. Compaction behavior of the MCC and granulations was also studied using a compaction simulator. RESULTS: In all cases, the wet granulation process decreased MCC primary particle porosity. Wet granulation also reduced

compactibility of MCC to different degrees. Overgranulated batch with HPC showed the lowest compactibility and was less compactible than the batch without HPC granulated using the same parameters. Ball-milled material showed an increase in porosity and was significantly more compactible than the unmilled granulation from the same batch. CONCLUSIONS: The decrease in MCC compactibility after granulation is associated with the decrease in MCC primary particle porosity and in some cases with the formation of large dense granules as well. Under certain conditions, milling seems to counteract the effect of wet granulation on MCC compactibility.

L14 ANSWER 20 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2005633177 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16246535
TITLE: The effect of crystal morphology and mill type on milling induced crystal disorder.
AUTHOR: Chikhalia V; Forbes R T; Storey R A; Ticehurst M
CORPORATE SOURCE: Drug Delivery Group, School of Pharmacy, University of Bradford, Bradford BD7 1DP, UK.
SOURCE: European journal of pharmaceutical sciences : official journal of the European Federation for Pharmaceutical Sciences, (2006 Jan) Vol. 27, No. 1, pp. 19-26. Electronic Publication: 2005-10-24.
Journal code: 9317982. ISSN: 0928-0987.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200603
ENTRY DATE: Entered STN: 30 Nov 2005
Last Updated on STN: 24 Mar 2006
Entered Medline: 23 Mar 2006

AB Milling is a key process in the preparation of many solid dosage forms. One possible milling induced change is the production of small levels of disorder or amorphous material found predominantly at the surface of a powder, which could lead to significant chemical and physical instability. The influence of crystal habit on this change was investigated using beta-succinic acid, in plate like and needle like morphologies. beta-Succinic acid crystals with these habits were processed in a ball mill and a jet mill. SEM images indicated jet milled material was finer than the ball milled product. Powder X-ray diffraction of the milled powders revealed an amorphous halo at lower angles and peak broadening suggesting disorder though this could not be quantified accurately. In addition, a partial conversion during milling to the alpha form was noted. Quantitation of the alpha form in the milled powders indicated it was present at <2% (w/w). Plate and needle shaped particles had similar heats of solution pre-milling, however, all milled powders had lower heats of solution compared to the unmilled powers. The contribution of the alpha polymorph to the lower heats of solution was calculated to be insignificant. Therefore, the reduced heat of solution is attributed to a loss in crystallinity. The largest decreases were seen in the plate like morphology. These findings suggest that beta-succinic acid crystals with plate like morphology are more prone to crystallinity loss on milling compared to the needle like morphology. The mill type has also been shown to influence the final crystallinity.

L14 ANSWER 21 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2005370482 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16028017

TITLE: Characterization of drug particle surface energetics and young's modulus by atomic force microscopy and inverse gas chromatography.

AUTHOR: Davies Michael; Brindley Anne; Chen Xinyong; Marlow Maria; Doughty Stephen W; Shrubb Ian; Roberts Clive J

CORPORATE SOURCE: Laboratory of Biophysics and Surface Analysis, School of Pharmacy, The University of Nottingham, NG7 2RD, Nottingham, UK.

SOURCE: Pharmaceutical research, (2005 Jul) Vol. 22, No. 7, pp. 1158-66. Electronic Publication: 2005-07-22.
Journal code: 8406521. ISSN: 0724-8741.

PUB. COUNTRY: United States

DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200602

ENTRY DATE: Entered STN: 20 Jul 2005
Last Updated on STN: 16 Feb 2006
Entered Medline: 15 Feb 2006

AB PURPOSE: Particulate interactions are dominated by aspects such as surface topography, exposed chemical moieties, environmental conditions, and thermodynamic properties such as surface free energy (gamma). The absolute value and relative magnitude of surface energies of a drug and excipients within a formulation can significantly influence manufacture, processing, and use. This study utilizes and compares the potentially complementary analytical techniques of atomic force microscopy (AFM) and inverse gas chromatography (IGC) in the quantitative determination of the surface energy of drug (budesonide) particles (micronized and unmilled) relevant to inhaled delivery. In addition, the study investigates with AFM another important parameter in determining material interactions, the local mechanical properties of the drug. METHODS: AFM was used to acquire force of adhesion (Fadh) and related work of adhesion (WA) and surface energy values between individual mironized drug particles and also model substrates (graphite and mica). In addition, AFM probes were used to interrogate the surface energy of unmilled drug particles. Measurement with AFM probes also yielded localized measurements of Young's modulus for the unmilled drug. IGC was also used to probe the surface characteristics of the bulk drug material. RESULTS: The average values for surface energies acquired from budesonide micronized particle interactions with graphite, mica, and drug particles of the same substance were found to range from 35 to 175, 5 to 40, and 10 to 32 mJ m(-2), respectively. The unmilled material displayed a range of values of 39-88 mJ m(-2) with an average of 60 mJ m(-2). The IGC result for the surface energy of the micronized material was 68.47 +/- 1.60 mJ m(-2). The variability in surface energy from AFM, a feature particularly apparent for the micronized material was attributed to two factors, intrinsic material variations within a single particle and assumptions present within the contact mechanics model used. Here we provide a detailed description of these factors to go some way to rationalize the results. The Young's modulus of the unmilled drug was determined to be approximately 10 GPa. CONCLUSION: The range of determined surface energies between the AFM measurement on graphite, mica, and the drug is proposed to reflect the different chemistries displayed by the drug at the single particle level. The maximum values of these ranges can be related to the sites most likely to be involved in adhesion. AFM and IGC yield surface energy estimates in approximate agreement, but clearly are interrogating surfaces in different fashions. This raises questions as to the nature of the measurement being made by these approaches and to the most appropriate time to use these methods in terms

of a direct relation to formulation design, manufacture, and drug delivery. Finally, we demonstrate a novel method for assessing the Young's modulus of a drug from a single particle.

L14 ANSWER 22 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2004232948 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15132178
TITLE: Insulin-loaded calcium pectinate nanoparticles: effects of pectin molecular weight and formulation pH.
AUTHOR: Cheng Kun; Lim Lee-Yong
CORPORATE SOURCE: Department of Pharmacy, National University of Singapore, Singapore.
SOURCE: Drug development and industrial pharmacy, (2004 Apr) Vol. 30, No. 4, pp. 359-67.
Journal code: 7802620. ISSN: 0363-9045.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 11 May 2004
Last Updated on STN: 15 Sep 2004
Entered Medline: 14 Sep 2004

AB Insulin-loaded calcium pectinate nanoparticles were prepared as a potential colonic delivery system by ionotropic gelation with calcium ions. The effects of pectin molecular weight (Mv) and formulation pH on the characteristics of the nanoparticles were evaluated. Commercial pectins, LM101 and LM104, with respective degrees of esterification of 36% and 28%, were depolymerized by mechanical milling to give Mv ranging from 89 to 5.6 kDa. Milled pectins did not yield nanoparticles with significantly different mean diameter and insulin association efficiency (AE) compared to nanoparticles of unmilled pectins. LM104 nanoparticles had smaller variation in mean size than the LM101 nanoparticles. Formulation pH significantly influenced the AE and stability of the nanoparticles. Increasing the pH from 2 to 3 enhanced the AE by three-fold, from 32.76% to 93.31%, at an insulin loading concentration of 80 U/mL. This increase in AE was correlated to the charge density on the pectin molecules as a function of pH. Subsequent release of associated insulin from the nanoparticles was dependent on the extent of dilution of the nanoparticle dispersion and the pH of the dissolution medium. Cross-flow filtration could be used to separate the nanoparticles from unassociated ions and molecules, without compromising the characteristics of the nanoparticles.

L14 ANSWER 23 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2002621540 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12378963
TITLE: Ultrafine grinding using a fluidized bed opposed jet mill: effects of feed load and rotational speed of classifier wheel on particle shape.
AUTHOR: Chan L W; Lee C C; Heng P W S
CORPORATE SOURCE: Department of Pharmacy, National University of Singapore, 10 Kent Ridge Crescent, Singapore 119260.
SOURCE: Drug development and industrial pharmacy, (2002 Sep) Vol. 28, No. 8, pp. 939-47.
Journal code: 7802620. ISSN: 0363-9045.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 17 Oct 2002
Last Updated on STN: 8 May 2003
Entered Medline: 7 May 2003

AB Circularity, aspect ratio, modelx, and pellips were employed to study the effects of process parameters, namely varying feed loads and rotational speeds of the classifier wheel, of the fluidized bed opposed jet mill on the shape of the micronized particles produced. The Shapiro-Wilk statistical test showed that 80.0% of the shape distributions of the four descriptors were not normal. Therefore, the Kruskal-Wallis test, which is a nonparametric statistical test, was employed to analyze the data. Micronized particles were more spherical and less elongated, as indicated respectively by higher median circularity and lower median modelx values when compared to unmilled lactose. These descriptors were able to indicate that the particles had been micronized. When feed loads of 250 and 350 g were used, increasing the rotational speed of the classifier wheel was found to bring about a decrease in span values of all the shape descriptors, indicating that the micronized particles were more uniform in shape. Micronized particles produced had lower median aspect ratio values than the unmilled lactose, whereas a higher feed load of 450 g resulted in the production of micronized particles that were less uniform in shape and more elliptical in nature, as reflected by the lower median pellips values. A higher feed load of 450 g caused a high level of impingement of particles on to the rotating classifier wheel, causing decreased classifier wheel efficiency, and this resulted in a less well-controlled micronization process. Thus, aspect ratio and pellips were sensitive to the changes in performance of the classifier wheel. The four shape descriptors were proposed to be used collectively as indicators for the monitoring of the micronization process.

L14 ANSWER 24 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2002045410 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11755273
TITLE: The impact of low levels of amorphous material (<5%) on the blending characteristics of a direct compression formulation.
AUTHOR: Mackin Lesley; Sartnurak Soisurin; Thomas Iwan; Moore Stephen
CORPORATE SOURCE: Pharmaceutical and Analytical Sciences, Pharmacia R&D, Chicago, IL 60077, USA.. lesley.mackin@astrazeneca.com
SOURCE: International journal of pharmaceutics, (2002 Jan 14) Vol. 231, No. 2, pp. 213-26.
Journal code: 7804127. ISSN: 0378-5173.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 24 Jan 2002
Last Updated on STN: 13 Feb 2002
Entered Medline: 12 Feb 2002

AB During the manufacture of tablets for registration stability studies, it was observed that blends manufactured using milled active frequently failed the blend content uniformity criteria (actual relative standard deviation (RSD) of 4-15%) at the prelubrication stage, whereas unmilled active batches were consistently giving very good blend uniformity results (RSD<3.5%). The addition of magnesium stearate dramatically improved the blending characteristics of the milled batches, suggesting that milling had altered the surface properties. A hypothesis was presented that amorphous material was created during the milling of

the active batches, which subsequently recrystallised over a short period of time e.g. days/hours. Following recrystallisation the batches did not exhibit the same physical properties as the unmilled actives, and this resulted in the drug product batches failing to meet their pre-lubrication acceptance criteria for blend content uniformity. This paper describes the results of a laboratory scale study to investigate this hypothesis and therefore explain the processing issues that were observed during the manufacture of the registration stability batches with milled active batches.

L14 ANSWER 25 OF 25 MEDLINE on STN
ACCESSION NUMBER: 93148132 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1491339
TITLE: Physical and lubrication properties of magnesium stearate.
AUTHOR: Leinonen U I; Jalonen H U; Vihervaara P A; Laine E S
CORPORATE SOURCE: Orion Corporation Farmos, Turku, Finland.
SOURCE: Journal of pharmaceutical sciences, (1992 Dec) Vol. 81, No. 12, pp. 1194-8.
Journal code: 2985195R. ISSN: 0022-3549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199303
ENTRY DATE: Entered STN: 12 Mar 1993
Last Updated on STN: 12 Mar 1993
Entered Medline: 4 Mar 1993

AB The lubrication properties of two commercial-grade magnesium stearates were studied. Their moisture contents and crystal structures were similar. There were minor differences in their fatty acid composition, but the differences did not affect the lubrication properties. The lubrication properties correlated with particle size distributions and specific surface area. The effect of these parameters was further studied with unmilled and milled chemically pure magnesium stearate. Milling decreased the particle size and increased the specific surface area. In both cases, the batch with a smaller particle size and larger specific surface area had considerably better lubricity.

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L3   22 S L1 OR L2
L4   4689 S FLUTAMIDE OR EULEXIN OR FLUTAMIN
L5   177751 S MILL OR MILLING OR UNMILLED OR MILLED
L6   5 S L4 AND L5
L7   21 S L1 NOT L6
L8   1 S UNMILLED (10A) L4
L9   461227 S PHARMACEUTICAL
L10   507 S UNMILLED
L11   27 S L9 AND L10
L12   26 S L11 NOT L6
L13   2 S L9 (20A) L10
L14   25 S L12 NOT L13